Scientific Research Publishing

Journal of Diabetes Mellitus, 2023, 13, 284-299
https://www.scirp.org/journal/jdm
ISSN Online: 2160-5858
ISSN Print: 2160-5831

The Principles of Insulin Management of Type 2 Diabetes Mellitus

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How to cite this paper: Kawa, L.B. and Alexander, H. (2023) The Principles of Insulin Management of Type 2 Diabetes Mellitus. *Journal of Diabetes Mellitus*, **13**, 284-299.
https://doi.org/10.4236/jdm.2023.134022

Received: July 19, 2023
Accepted: November 18, 2023
Published: November 21, 2023

Abstract

Insulin therapy is an integral part of the pharmacological management of Type 2 diabetes mellitus. Guidelines recommended insulin therapy for those patients with suboptimal glycaemic control despite optimal medical treatments. Studies show that insulin therapy with the human and regular insulins improve glycaemic control, reduce the chronic complications, and inevitably improve patient's quality of life. The new analogue insulin has a better safety profile and efficacies, and has been shown to achieve better outcomes and patient's acceptability compared with the human and regular insulins. The diabetic guidelines also recommend the intensity of insulin therapy in a personalised glycaemic control strategy based on the patient's profiles and their preferences. However, the guidelines do not recommend any standardised approach to the principles of insulin initiation, titration, and monitoring. This review summarises the essential principles of insulin initiation, titration, and monitoring in Type 2 diabetes mellitus.

Keywords

Insulin, Type 2 Diabetes, Principles of Insulin Therapy

1. Introduction

The isolation of insulin is one of the greatest medical discoveries of the last century [1]. It has changed the face of Type 1 Diabetes Mellitus (T1DM) from a fatal condition to a chronic manageable disease [1] [2] [3] and thanks to this discovery millions of people are alive today.

Insulin therapy has also been extended to the management of Type 2 diabetes mellitus (T2DM) either to augment or replace endogenous insulin, since 30% - 50% of glycaemic control in T2DM patients are suboptimal despite being on op-

timal medical treatments [4].

The insulin's main advantage over other glucose lowering treatments is that it lowers glucose over wide range to almost any targets limited by hypoglycaemia. Studies with human and regular insulin therapy in T2DM have shown that insulin treatment improves glycaemic control and reduces chronic complications of T2DM [5] [6]. For example, the United Kingdom Prospective Diabetes Study (UKPDS) was a study assessing intensive glycaemic treatment strategy in T2DM using oral hypoglycaemic agents plus insulin. The insulin arm achieved better glycaemic control compared with the other treatment arms [5]. However, this was associated with a 1.8% severe hypoglycaemias per year and a 4 kg weight gain compared with other treatments [5]. The KOMOMOTO trial in Japan was an insulin alone treatment among hundred and ten T2DM patients, fifty-five with background retinopathy and fifty-five without retinopathy. It compared the effects of intensive insulin with multiple injection therapy versus standard insulin twice daily therapy. The result showed that the intensive regimen delayed microvascular complications [6].

Although, these studies were designed to assess the effects of intensive insulin strategy with the human insulin, the results show that insulin therapy in T2DM with or without other treatments, optimises glycaemic control and delays the chronic complications at the expense of severe hypoglycaemic episodes and weight gains.

Comparative trials have shown that the analogue insulin improves the glycaemic control with less hypoglycaemic episodes, less weight gain and more patient acceptability compared with the human insulins [7] [8] [9]. With its peculiar pharmacological profile, analogue insulin reduces the frequencies of injection and accommodates flexible meal times. The use of analogue insulin is, therefore, the current trend in the management of T2DM.

The contemporary guidelines for the treatment of T2DM recommend a personalised glycaemic treatment strategy based on the patient's clinical profile and preferences [10] [11] [12] with insulin as a second- or third-line therapy for patients with suboptimal glycaemic control despite optimal oral treatments [10] [11] [12]. There are, however, other indications for insulin therapy including signs of glucotoxicities, glycated haemoglobin A1c (HBA1c) ≥ 9%, random blood glucose ≥ 16 mmol/L, ketosis and those who have acute myocardial infarction [13] [14]. Recent evidence, also suggests that even early treatment of T2DM with insulin as a first line treatment in the newly diagnosed T2DM patients could preserve the β cell function, reduces glucotoxicity, lipotoxicity, insulin resistance and results in the remission of diabetes [15] [16].

The guidelines, however, do not provide the principles of initiation, titration, and the monitoring of the insulin therapy. These can pose significant challenge for prescribers who have limited knowledge and experiences in prescribing and monitoring insulin therapy. This paper reviews the role of insulin in the management of T2DM with the objectives of highlighting the suitable types of insu-

lins, glycaemic strategy and the essential principles of initiation, titration, and monitoring in T2DM.

2. Role of Insulin Therapy in Type 2 Diabetes Mellitus

Insulin is currently recommended in the guidelines as a second or third-line treatment of the T2DM patients. Significant number of patients with T2DM has poor glycaemic control despite being on optimal glucose lowering drugs and lifestyle modifications [4]. Insulin is therefore used in the management of diabetes to archive glycaemic control, prevent, or reduce chronic complications and maintain quality of life. It is prescribed to either augment or to replace deficient endogenous insulin.

2.1. Augmentation

Insulin a*ugmentation* is used in those T2DM patients to complement the endogenous insulin secretion by overcoming the resistance at the peripheral insulin dependent organs (liver, muscles, and kidneys). It is initiated at the rate of 0.3 - 0.5 units/kg either as basal or as bolus insulin after meals. In a specific study where, premix, bolus and the long-acting insulins were used to argument endogenous insulin, the group receiving the long-acting insulin group had less weight gain and hypoglycaemic episodes than the other two groups. However, the glycaemic control was better with both the bolus and long-acting basal insulin [17]. This suggests that either type of insulin can be prescribed depending on the patient's preferences, their clinical profile, and the availability.

2.2. Replacement

Insulin replacement is predominantly used in the management of T1DM. However, it is recommended in T2DM whose glycaemic control is suboptimal despite on optimal treatments and in those who develop signs of glucotoxicity. These groups of patients could be insulin deficient reaching a burnt-out stage of their β cell function. Deficient plasma C-peptide levels would be reasonable to establish before insulin therapy. However, this approach is used seldom in the clinical practice, so patients are generally commenced on replacement therapy without the assessment of plasma c-peptide level.

Replacement insulin is initiated at the rate of 0.6 - 1 units/kg with different regimens such as the basal bolus or premix with 50% of the total body requirement administered as basal and the other 50% is divided equally during big meals. Replacement with continuous insulin infusion via a pump (CIIP) is used in those with erratic plasma glucose control.

3. Principles of Insulin Initiation

Insulin is secreted in a bimodal fashion by a normal functioning pancreas and the use of exogenous insulin is an attempt to simulate this function. The insulin therapy in T2DM is initiated when plasma glucose is poorly controlled, or a

clinical decision is made by the treating physician that a newly diagnosed patient can be insulinsed early for possible remission with good outcome [15] [16]. Although, there are no specific standards for insulin therapy, there are however, several caveats that needed to be considered before the initiation. Firstly, patients with T2DM, must meet the clinical criteria for the initiation [10] [14]. Secondly, the type of insulin, the doses, the regimen, and the monitoring process are considered. Thirdly, the intensity of insulin therapy (aggressive vs standard) based on a pretreatment glycaemic target that suits the patients' clinical profiles and their preferences [18] [19].

The insulin analogues have significantly improved this aspect of treatment customisation. The analogues have better efficacy, safety, patients' acceptance, optimal dosages and flexible regimens [7] [8] [20] compared with the human insulins. Its fixed dose combinations improve glycaemic control with less episodes of hypoglycaemia and weight gains prevalent with human insulin therapy [21]. Finally, patient education about the insulin, the side effects, the change of dosages according to their prevailing plasma glucose levels, travel, fasting, and the sick day rules information on access to urgent healthcare if needed. This review covers the first three caveats as the fundamental principles in the consideration of insulin therapy in T2DM.

3.1. Criteria for Initiation of Insulin

Insulin initiation and titration for patients have always remained a challenge for both the patients and their physicians [21] due to multifactorial patients and physician factors. This has led to the perception that insulin therapy in T2DM is the last therapy. This perception is also based on the pathophysiology of T2DM as being relatively deficient in insulin function and that early insulisation is not needed until late. The corollary is demonstrated on the treatment guidelines where insulin appears as either a second and or third line treatment [11] [12]. This therefore contributes approximately 30% - 50% of patients with T2DM to live with suboptimal glycaemic control for years [4].

Recent studies have shown that "early insulinisation" leads to the preservation of the β cells and better clinical outcomes including in some cases, the clinical remission of T2DM [15] [16] [22]. On the contrary, the late insulin therapy as it is in the current practice, misses the opportunity to preserve the β cell function and achieve clinical remission of T2DM. This demonstrates physician's clinical inertia and, in some cases, patient's psychological inertia that can promulgate uncontrolled glycemia for years leading to chronic complications [16] [23]. In fact, late insulin therapy to attain aggressive glycaemic control in patients with long duration of diabetes with established chronic complications has been shown to increase mortality [22]. Thus, early insulin therapy should be considered in the newly diagnosed T2DM patients with no chronic complications.

Patient's clinical criteria play a very important basis for the consideration of insulin therapy in T2DM. These criteria include the clinical signs and symptoms

of glucotoxicity (polyuria, polydipsia, polyphagia, and weight loss), suboptimal glycaemic control despite optimal therapy, HBA1c ≥ 9% (11.7 mmol/L), random blood sugar (RBSL) ≥ 16 mmol/L [13], ketosis and acute myocardial infarction [14].

Additional criteria are important to consider with the clinical criteria. Patient's clinical profile, functional status, their social and educational status assessment are critically important in the decision and planning processes. For, example a T2DM requiring insulin but has arthritic hands and lives alone would require further planning of support for injection and monitoring so as a blind person. Patients' ability to self-administer insulin and their knowledge about the insulin doses, effects, and few general rules around daily uses in travel, sports, fasting, and alcohol are important to consider and identified gaps be optimised before treatment.

3.2. Choosing the Correct Insulin Type, Dose, and Regimen

3.2.1. Choosing the Correct Insulin

Analogue insulin provides better glycaemic control, reduces hypoglycaemic episodes and weight gain commonly associated with the regular human insulin. Rosenstock *et al.*, in their study comparing daily insulin glargine and twice daily neutral protamine hagedorn (NPH) insulin among five hundred and eighteen NPH treated with or without prandial regular insulin T2DM patients showed that glargine was effective in glycaemic control, reduced nocturnal hypoglycaemic episodes and less weight gain compared to NPH insulin as basal insulin [8].

Prandial insulin with analogue insulin compared with regular insulin also shows better outcomes. Chlup *et al.* have compared the effects of switch from regular human insulin to aspart insulin with equivalent doses among fifty-seven T2DM patients. They showed that aspart insulin was effective in glycaemic control with greater acceptability by the patients than the regular human insulin [7].

APPOLO trial was an open parallel comparative randomised trial of the long basal analogue glargine and short acting prandial analogue insulin lispro. This trial attempted to show if there were any differences between glycaemic control and patient's acceptability of the types of analogue insulins. It recruited four-hundred and fifteen T2DM suboptimally controlled with oral hypoglycaemic agents and randomised to either glargine once daily vs lispro three times daily. It concluded that, although glycaemic control was better in both treatment arms, glargine was simple, effective, and more satisfactory for patients in the initiation of therapy. This was due to lower risk of hypoglycaemia, fewer injections, less glucose monitoring, and greater acceptance compared with the short acting prandial lispro [24]. Therefore, basal long-acting analogue are better than the short acting prandial lispro.

Collectively, these studies therefore show that basal plus or basal bolus insulin with the analogues are better than the basal alone with the long-acting basal analogue insulin or the NPH insulin. However, based on the APPOLO trial, basal long-acting analogue insulin is therefore recommended as the first line in-

sulin therapy by a joint statement from the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) [20].

Despite this evidence and the recommendations, the analogue insulins are not available in some health care systems in the world due to costs. The first author of this review worked in a system that does not have the analogues on the government public pharmaceutical system and human and regular insulins are used instead. This reduces the suitable options available to the prescribers and their patients. The best choice of insulin in such situations is best agreed by consensus with the patients.

The pharmacokinetic profile of different insulins is one of the critical determinants that enable the prescribers in choosing the correct insulin for patients with T2DM (**Table 1**).

3.2.2. Choosing the Correct Insulin Dose

There are no standardised insulin dosages to initiate in patients with T2DM. It depends on the clinical experience of the prescriber and the prevailing plasma glucose level. For example, an estimated basal unit of insulin can be commenced using the augmented or the replacement doses as the starting dose depending on the glucose level and the dosage escalated by 2 units until basal and postprandial glycaemic control are achieved. Further, patients' profiles such as their weight, insulin sensitivity and carbohydrate count ratios can also be used to estimate the insulin dosages and requirement. **Table 2** shows the tentative insulin dose calculation.

3.2.3. Choosing the Correct Insulin Regimens

Six different insulin regimens are currently used in the management of the T2DM. A desirable insulin regimen is based on the patient's clinical profile, preference and has the pharmacokinetic profile that mimics the endogenous insulin secretion that will reproduce desirable glycaemic control.

Evidence supporting any specific insulin regimens for the management of the T2DM patients with or without baseline optimal oral hypoglycaemic agents is limited. To determine a suitable insulin regime, the 4-T Study recruited seven hundred and eight T2DM patients optimally treated with sulphonylurea and metformin. The insulin regimens were basal detemir, premixed biphasic aspart and prandial bolus aspart insulin. Hypoglycaemia was more common among those who received the pre-mixed and bolus insulin than basal insulin. However, weight gain was more common among those who received basal insulin than those who received premix or bolus insulins [17].

In a comparative randomised trial of T2DM patients who were receiving NPH as basal insulin with or without regular prandial insulin, the group that changed to the first-generation analogue insulin glargine-100 as basal regimen has achieved effective glycaemic control with less weight gains and hypoglycaemic episodes compared with the group with NPH group [8].

The second-generation basal insulin analogue of Glar-300 and Degludec 100

Table 1. Pharmacokinetics of different classes of insulins and time to use.

Insulin Class*	Onset of action	Peak	Duration of action	When to Use
Ultra short Acting*	15 mins	1 hour	2 - 4 hours	Administered at mealtimes, just before or after the meals
Lispro (Humalog)†	15 mins	30 - 90 mins	3 - 5 hours	
Aspart (Novarapid)†	15 mins	1 - 3 hours	4 - 5 hours	
Glulisine (Aphidra)	15 - 30 mins	30 - 60 mins	4 hours	
Short acting*	30 min	2 - 3 hours	3 - 6 hours	Administered 30 mins before meals or after if unpredictable
Humulin S (Actrapid)	30 mins	1.5 - 2.5 hours		
Insuman Rapid	30 mins			
Intermediate Acting*				
Humulin *Human insulatard* *Isophane*	2 - 4 hours	4 - 12 hours	12 - 18 hours	Administered twice daily. Not dependent on meals
Long Acting*	2 hours	Do not peak	Up to 24 hours	Administered once a day and not dependent on meals
Glargine	6 hours	No peak	24 hours	
Determir	1 - 2 hours	No peak	14 - 24 hours	
Degludec	1 - 2 hours	No peak	>40 hours	
Fixed Dose*	5 - 6 mins	Variable peaks	10 - 16 hours	Administered twice daily with food as basal insulin plus regimen
Humalog Mix	30 - 60 mins	(Lispro + Protamine)	10 - 16 hours	
• 25 *(Lispro + Protamine)*				
• *Humalog Mix* 50 *(Lispro + Protamine)*				
Novamix (Aspart + Protamine)	5 - 15 mins	Dual (Protamine + Aspart)	10 - 16 mins	
• *Novamix* 30				
• *Novamix* 50				
NPH (Isophane + Regular insulin)	30 - 60 mins	Dual (NPH/Regular)	10 - 16 hours	
• 70/30				
• 50/50				
Mixtard (soluble insulin + Isophane)	30 mins	Dual (soluble insulin + Isophane)	10 - 16 hours	
• 30/70				
• 40/60				
• 50/50				
Degludec/Aspart (70/30)	15 mins	Dual (Degludec + Aspart)	>40 hours	

*Times are approximate and assume subcutaneous. The effects can vary depending on several factors such as injection technique and factors affecting absorption. †Lispro and aspart are also available in premixed forms with intermediate-acting insulins.

Table 2. Insulin dose calculation.

Criteria	Definition	Dosage
Argumentation	Argumentation of relative insulin deficiency with basal or bolus insulin	0.1 - 0.5 units/kg
Replacement	Replacement of absolute insulin deficiency with either in T1DM or T2DM with, basal, premix or bolus insulin	0.6 - 1 units/kg
Carbohydrate Count	Amount of insulin units estimated to cover ingested carbohydrate	500 g of carbohydrate divided by total daily insulin requirement
Insulin sensitivity/ Correction Factor	1 unit of insulin estimated to normalise glucose to defined level	100 divided by total daily insulin dose

units/ml have once daily injections and have lower incidences of hypoglycaemia. In a non-inferiority trial, Garber *et al*., have shown that T2DM patients who have received both second generation insulin with mealtime aspart have similar glycaemic control and side effects [9].

The Basal Plus regimen even have effective glycaemic control and less hypoglycaemic episodes than the basal regimen alone [17]. The coformulated insulin Degludec and insulin aspart are suitable for this regimen. The premixed insulins could be better for those who require a simple regimen. These findings suggest that different insulin regimens with analogue insulin are better in glycaemic control with less weight gains and hypoglycaemic episodes. The second generation long-acting basal analogue insulins are better than the first generation in a basal insulin regimen. They are more tolerable and accepted by patients with reduced daily injections than the regimens with human and regular insulins. The different insulin regimens are discussed separately under their subheadings below.

1) Once daily basal insulin regimen

This regimen is commonly used for argumenting basal endogenous insulin. The long-acting basal insulin (glargine, detemir, and degludec) or intermediate-acting insulin, such as isophane insulin (Humulin I or Insulatard) and or premix insulin are used in addition with the oral hypoglycaemic agents to control the steady state (basal glucose) between meals and overnight. The first-generation insulin analogues Glargin-100 (Glar-100) and insulin determir 100 units/ml provide 24-hour glucose control with low variability and hypoglycaemic effects compared with the NPH insulin [9]. The recently approved second generation long-acting analogues Glargin-300 (Glar-300) and Insulin Degludec 100 units/ml (IDec U100) or Degludec-200 units/ml (IDec U200) provide 48 hour glucose control with once daily doses and have lower incidences of hypoglycaemia compared with the first generation [9] [25] [26] [27].

2) Basal-Plus regimen

This regimen consists of a basal insulin with additional rapid prandial insulin after meals to control the postprandial glucose surge. Compared with a basal insulin regimen, this regimen has shown to be better [17], effective [25] and achieves better glycaemic control in reducing HBA1c [17]. Insulin degludec co-formulated with insulin aspart has been shown to improve glycaemia with less hypoglycaemia [28] and could be used in this regimen.

3) Premix insulin regimen

The pre-mixed regimen is composed of a mixture of basal intermediate insulin and a rapid-acting insulin administered twice daily as a simple regimen for those needing a simple regimen like the elderly, visually impaired and or in insulin naive patients starting treatment. This regimen is disadvantaged by poor glycaemic control, increased hypoglycaemia and reduces patients' flexibility in timing of their meals. It is rigid and must be taken with fixed meal schedules. However, it may be the only simple option available in some health care systems in the world.

4) Basal bolus insulin

This regimen refers to a long-acting or intermediate basal insulin for basal sugar control and a short acting insulin administered before a large meal. Studies have shown that there are no differences in glycaemic control or hypoglycaemic episodes between the long-acting glargine + lispro compared with pre-mix glargine/lispro in T2DM [29] [30]. Additionally, there were no increased insulin doses between this premix and basal insulin. However, basal bolus doses with analogue insulins had lower episodes of hypoglycaemia and less daily injections compared with the NPH insulin in patients with T1DM [31]. The use of analogue insulin in this regimen in T2DM appears to provide better glycaemic control and reduced hypoglycaemic episodes.

5) Basal insulin/incretin combinations

There are two patterns of this strategy: Glucagon-like peptide-1 receptor agonists (GLP1-RA) on insulin or insulin on GLP1-RA. Collectively, these combinations have improved the glycaemic control, reduced hypoglycaemia and weight gain seen among insulin treated patients [32] [33]. In addition, insulin doses have been reduced [33] and β cell destruction delayed [34] [35]. GLP1-RA and insulin in this regimen complement each other. The GLP1-RA negate insulin's untoward effects such as weight gain and hypoglycaemic episodes. The effect of the GLP-1RA on the reduction of the postprandial glycemia expedites reduction in insulin dosages.

6) Continuous subcutaneous insulin infusion pump (CSIIP)

Patients whose blood sugar fluctuates wildly despite multiple daily insulin injection regimen therapy qualify for CSIIP. Currently, many young and middle-aged people are the users of CSIIP [36]. The use of CSIIP stabilises glycaemic surges and control. This is currently prescribed by a qualified diabetic physician and/or endocrinologist in the United Kingdom. The machine costs between £2000 and £3000 depending on the supplier.

4. Glycaemic Strategy with Insulin

A pre-treatment glycaemic target measured by HBA1c level is an important pre-requisite for insulin therapy. It will determine how intense the insulin therapy is administered to achieve the target. It must be based on the patient's clinical profile to ensure patient safety because an aggressive glycaemic control with insulin can be detrimental to certain populations of T2DM.

An aggressive glycaemic control strategy is where HBA1c is set at ≤7% with an intensive insulin regimen. This strategy is suitable for young patients with diabetes with no complications and disabilities (**Figure 1**). The less intensive glycaemic strategy is where HBA1c target is set at a target between 7.1% and 8% with less intensive insulin therapy. This strategy is suitable for patients with long standing T2DM (>8 years), elderly, presence of chronic complications and disabilities.

Studies have shown that, patients with T1DM [37] [38] and T2DM [5] [6] [39]

who have had aggressive glycaemic control strategy had reduced chronic complications compared with the standard less intense glycaemic control. The Diabetes Control and Complication Trial (DCCT) analysed the impact of intensive insulin treatment on the microvascular complications versus less intensive treatment of two thousand, one hundred and forty-six T1DM patients with and without baseline diabetic retinopathy. The aggressively treated group had a 76% reduction in the development of retinopathy among patients with no background retinopathy and slowed the progression of retinopathy among those with background retinopathy by 54%. Additionally, microalbuminuria was reduced by 39% and clinical neuropathy by 60% in both cohorts in the aggressive management strategy [37]. Similarly, the smaller Stockholm Diabetes Intervention Study recruited one hundred and eight T1DM patients for an intensive versus less intensive insulin therapy. It showed significant reduction in the progression of the microvascular complications among those receiving intensive insulin treatments [38]. The secondary analysis also showed a strong correlation between aggressive control and the delay in complications overtime. These trials, unequivocally show that the aggressive glycemic control with intensive insulin management strategy of T1DM reduces and slows the progression of the microvascular complications.

This trend was replicated in the management of the T2DM in different populations. The UKPDS showed that intensive glycaemic control with sulfonylurea, metformin and insulin reduced overall microvascular complications by 25% [5]. The smaller Kumamoto trial in Japan among the T2DM also show a significant cumulative reduction in retinopathy and nephropathy among the Japanese patients with type 2 diabetes [6]. Furthermore, the ADVANCE Trial, of eleven thousand one hundred and forty T2DM patients showed that those who underwent an aggressive glycaemic strategy, had a combined 10% relative risk reduction in macrovascular and microvascular complications after 5 years primarily due to a 21% relative risk reduction [39].

This positive trend of the aggressive glycaemic strategy was however, countered by the findings from the Action to Control Cardiovascular Risks in Diabetes (ACCORD) Trial. In this trial, ten thousand two hundred and fifty-one patients with a mean age of sixty-two years and a mean HBA1c level of 8% were assigned to an intensive regimen (HBA1c < 6%) versus standard regimen (HBA1c 7% - 7.9%). There was increased mortality after 3.5 years among those in the intensive treatment arm. Additionally, there were no reductions in the chronic complications [22]. Subgroup analysis of the study showed that the increased mortality was predominantly among the elderly patients who had long standing diabetes and established chronic complications [22]. This led to the concept of 'personalised' diabetic treatment of individual diabetic patients where the intensity of their glycaemic control targets is specific to their individual clinical profiles. The current diabetes guidelines attest to this percept with the principle of 'personalised treatment' (**Figure 1**).

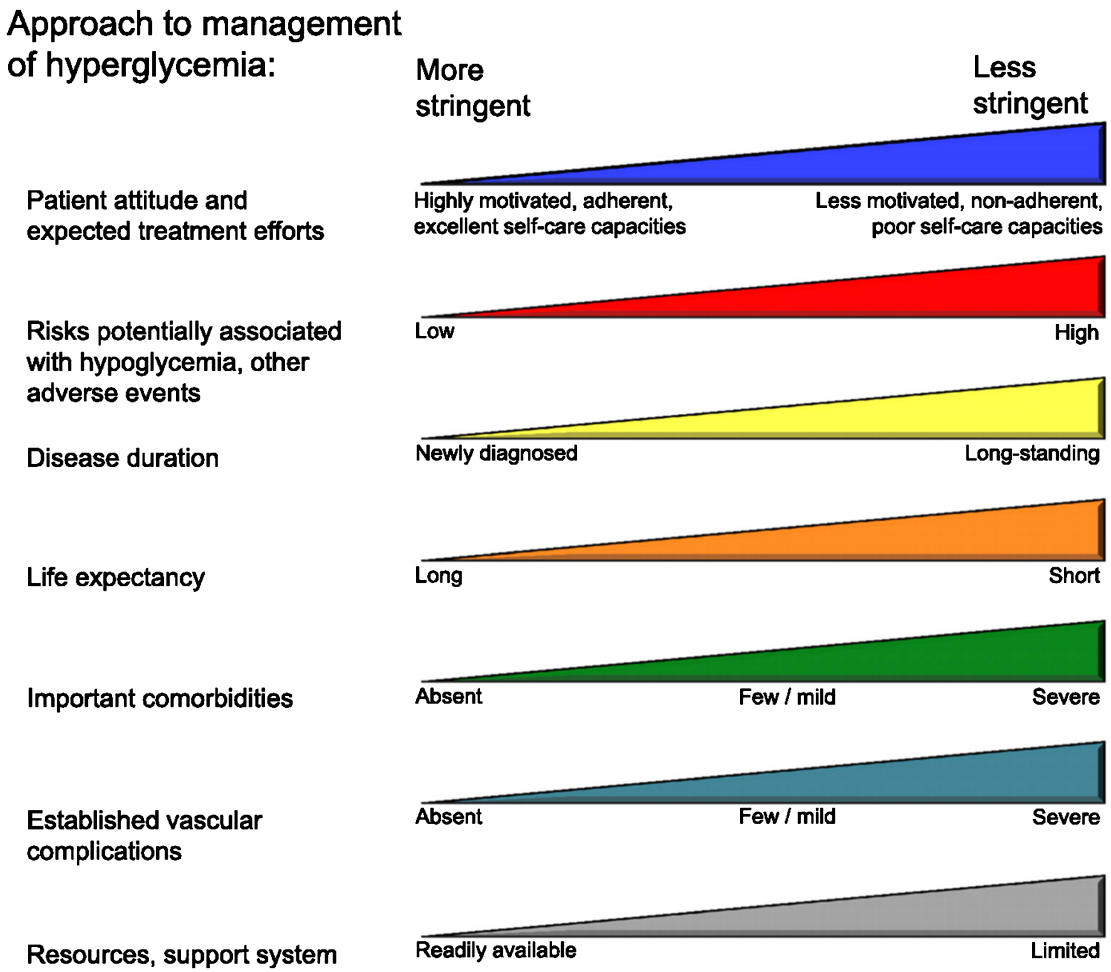

Figure 1. Personalised glycaemic control in treatment of Diabetes. Adapted from Silvio E. Inzucchi, *et al.* [11].

5. Monitoring and Titration

Monitoring and the titration of doses to achieve pre-treatment glycaemic target is critical to prevent the chronic complications. Studies have shown that titration helps to achieve glycaemic control and reduce the chronic complications [26] [40]. Thus, it is imperative that patients and possibly their careers be trained to monitor their own glucose to escalate and or de-escalate their insulin doses as necessary according to their prevailing glucose levels. This also encourages the patients to be in control of their own condition. Keeping a record book of glucose levels in the first few weeks of insulin initiation to adjust basal and the postprandial glucose will help in the titration process to archive pre-treatment glycaemic target.

6. Conclusions

Insulin therapy in T2DM is important in achieving glycaemic control, reducing chronic complications and maintaining patients' quality of life. The treatment guidelines of T2DM recommend insulin as a second or third-line treatment in those with suboptimal glycaemic control despite optimal medical treatments.

However, early insulin treatment also demonstrates preservation of β cell function and remission of overt T2DM.

The guidelines also recommend a personalised glycaemic management strategy based on the patient's clinical profile to reduce complications and improve clinical outcomes. The insulin intensity is based on this personalised glycaemic strategy. Aggressive insulin therapy (HBA1c ≤7%) is suitable for the young, short duration of diabetes with no complications and or disabilities whilst the less intense strategy (HBA1c 7.1% - 8%) is suitable for the elderly with long duration of diabetes, chronic complications, and disabilities.

To achieve the personalised glycaemic control, the prescriber needs to understand and apply the principles of insulin initiation, titration, and monitoring. The analogue insulin is the standard insulin used in the contemporary practice in the management of T2DM based on its efficacy, safety profile and patients' acceptability compared with the human and regular insulins. Different insulin regimens are also determined by patients' clinical profile and preferences with the long-acting basal analogue as an optimal regimen. Additional Plus or Bolus is added when further prandial glycaemic control is required. There is, however, no standard insulin dose for the initiation. That is estimated according to the argumentation or replacement approach or from several other caveats such as the clinical experience of the prescriber, weight of the patient, carbohydrate count and insulin sensitivity.

Declaration

Kawa LB has written the manuscript. Alexander H has proofread the manuscript and recommended edition. Both have agreed on the final draft for submission.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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